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16. ABSTRACT

This report summarizes and evaluates information relevant to a preliminary interim assessment of adverse health effects associated with specific chemicals or compounds. The Office of Emergency and Remedial Response (Superfund) uses these documents in preparing cost-benefit analyses under Executive Order 12991 for decision-making under CERCLA. All estimates of acceptable intakes and carcinogenic potency presented in this document should be considered as preliminary and reflect limited resources allocated to this project. The intent in these assessments is to suggest acceptable exposure levels whenever sufficient data are available. The interim values presented reflect the relative degree of hazard associated with exposure or risk to the chemical(s) addressed. Whenever possible, two categories of values have been estimated for systemic toxicants (toxicants for which cancer is not the endpoint of concern). The first, RfD_S or subchronic reference dose, is an estimate of an exposure level that would not be expected to cause adverse effects when exposure occurs during a limited time interval. The RfD is an estimate of an exposure level that would not be expected to cause adverse effects when exposure occurs for a significant portion of the lifespan. For compounds for which there is sufficient evidence of carcinogenicity, q_1^*s have been computed, if appropriate, based on oral and inhalation data if available.

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PREFACE

This report summarizes and evaluates information relevant to a preliminary interim assessment of adverse health effects associated with naphthalene. All estimates of acceptable intakes and carcinogenic potency presented in this document should be considered as preliminary and reflect limited resources allocated to this project. Pertinent toxicologic and environmental data were located through on-line literature searches of the TOXLINE, CANCERLINE and the CHEMFATE/DATALOG data bases. The basic literature searched supporting this document is current up to May, 1987. Secondary sources of information have also been relied upon in the preparation of this report and represent large-scale health assessment efforts that entail extensive peer and Agency review. The following Office of Health and Environmental Assessment (OHEA) sources have been extensively utilized:

U.S. EPA. 1980a. Ambient Water Quality Criteria for Naphthalene. Prepared by the Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office, Cincinnati, OH for the Office of Water Regulations and Standards, Washington, DC. EPA-440/4-80-059. NTIS PB 81-117707.

U.S. EPA. 1982. Revision and Update of Hazard Profile on Naphthalene. Prepared by the Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office, Cincinnati, OH for the Office of Solid Waste and Emergency Response, Washington, DC.

U.S. EPA. 1983. Reportable Quantity Document for Naphthalene. Prepared by the Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office, Cincinnati, OH for the Office of Emergency and Remedial Response, Washington, DC.

U.S. EPA. 1986a. Health and Environmental Effects Profile for Naphthalene. Prepared by the Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office, Cincinnati, OH for the Office of Solid Waste and Emergency Response, Washington, DC.

U.S. EPA. 1986b. Summary Review for Health Effects Associated with Naphthalene: Health Issue Assessment. Prepared by the Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office, Research Triangle Park, NC for the Office of Air Quality Planning and Standards and the Office of Air and Radiation, Washington, DC.

The intent in these assessments is to suggest acceptable exposure levels for noncarcinogens and risk cancer potency estimates for carcinogens whenever sufficient data were available. Values were not derived or larger uncertainty factors were employed when the variable data were limited in scope tending to generate conservative (i.e., protective) estimates. Nevertheless, the interim values presented reflect the relative degree of hazard or risk associated with exposure to the chemical(s) addressed.

Whenever possible, two categories of values have been estimated for systemic toxicants (toxicants for which cancer is not the endpoint of concern). The first, RfD_S (formerly AIS) or subchronic reference dose, is an estimate of an exposure level that would not be expected to cause adverse effects when exposure occurs during a limited time interval (i.e., for an interval that does not constitute a significant portion of the lifespan). This type of exposure estimate has not been extensively used, or rigorously defined, as previous risk assessment efforts have been primarily directed towards exposures from toxicants in ambient air or water where lifetime exposure is assumed. Animal data used for RfD_S estimates generally include exposures with durations of 30-90 days. Subchronic human data are rarely available. Reported exposures are usually from chronic occupational exposure situations or from reports of acute accidental exposure. These values are developed for both inhalation (RfD_{SI}) and oral (RfD_{SO}) exposures.

The RfD (formerly AIC) is similar in concept and addresses chronic exposure. It is an estimate of an exposure level that would not be expected to cause adverse effects when exposure occurs for a significant portion of the lifespan [see U.S. EPA (1980b) for a discussion of this concept]. The RfD is route-specific and estimates acceptable exposure for either oral (RfD_O) or inhalation (RfD_I) with the implicit assumption that exposure by other routes is insignificant.

Composite scores (CSs) for noncarcinogens have also been calculated where data permitted. These values are used for identifying reportable quantities and the methodology for their development is explained in U.S. EPA (1984).

For compounds for which there is sufficient evidence of carcinogenicity RfD_S and RfD values are not derived. For a discussion of risk assessment methodology for carcinogens refer to U.S. EPA (1980b). Since cancer is a process that is not characterized by a threshold, <u>any</u> exposure contributes an increment of risk. For carcinogens, q_1^*s have been computed, if appropriate, based on oral and inhalation data if available.

ABSTRACT

In order to place the risk assessment evaluation in proper context, refer to the preface of this document. The preface outlines limitations applicable to all documents of this series as well as the appropriate interpretation and use of the quantitative estimates.

An RfD_{SO} and RfD_{O} for naphthalene of 29 mg/day was derived from a chronic dietary study in rats. Data were insufficient for derivation of an RfD_{SI} or RfD_{I} for naphthalene. A CS of 13.2 was based on kidney lesions in rats in a subchronic gavage study.

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LIST OF ABBREVIATIONS

ADI	Acceptable daily intake
BCF	Bioconcentration factor
CAS	Chemical Abstract Service
CS	Composite score
K_{oc}	Soil sorption coefficient
MED	Minimum effective dose
NOEL	No-observed-effect level
PAH	Polycyclic aromatic hydrocarbons
PEL	Permissible exposure limit
ppm	Parts per million
RFD	Reference dose
RFD_I	Inhalation reference dose
RFD_O	Oral reference dose
RFD_S	Subchronic reference dose
RFD_{SI}	Subchronic inhalation reference dose
RFD_{SO}	Subchronic oral reference dose
RQ	Reportable quantity
RV_d	Dose-rating value
RV_e	Effect-rating value
STEL	Short-term exposure limit
TLV	Threshold limit value
TWA	Time-weighted average

1. ENVIRONMENTAL CHEMISTRY AND FATE

The physical and chemical properties and environmental fate of naphthalene (CAS No. 91-20-3) are as follows:

Chemical class:	polycyclic aromatic hydrocarbon
Molecular weight:	128.19 (Callahan et al., 1979)
Vapor pressure at 25°C::	0.082 mm Hg (MacKay et al., 1982)
Water solubility at 25°C:	31.7 mg/ℓ (MacKay et al., 1980)
Log octanol/water partition coefficient:	3.30 (Hansch and Leo, 1985)
K_{oc}:	1288 (Sabljic, 1984)
BCF:	20-567 (U.S. EPA, 1986a; Correa and Venables, 1985)
Half-lives in Air:	8-12 hours (U.S. EPA, 1986a)
Water:	2.3 days (Zoeteman et al., 1980)
Soil:	3.6 months (U.S. EPA, 1986a; NLM, 1987)

The dominant removal mechanism for napthalene in air is predicted to be reaction with photochemically generated hydroxyl radicals. In photochemical smog situations, reaction with NO_3 radicals is expected to occur but the half-life of this process (15 hours) is longer than the half-life because of its OH radical reaction (8-12 hours) (U.S. EPA, 1986a). Significant removal from the atmosphere by wet or dry deposition is unlikely (U.S. EPA, 1986a).

The removal of naphthalene from a shallow, rapidly flowing stream is predicted to be as follows: volatilization, 80%; sediment sorption, 15.5%;

microbial degradation, 4.4%; photolysis, <1% (U.S. EPA, 1986a). Bioaccumulation in aquatic organisms is not expected to be significant (U.S. EPA, 1986a; NLM, 1987). The aquatic half-life reported (Zoeteman et al., 1980) is for the overall half-life of naphthalene in a river.

Naphthalene is adsorbed moderately to soil and is expected to biodegrade. Biodegradation may be rapid in soils previously contaminated with PAHs (half-life hours to days) but will be slow otherwise (NLM, 1987). Significant amounts of naphthalene may be lost by volatilization from soil surfaces. Groundwater contamination has been detected at waste disposal sites and spill sites (U.S. EPA, 1986a). The estimated volatilization half-life of naphthalene from a soil containing 1.25% organic carbon was 1.1 day at a depth of 1 cm and 14 days at a depth of 10 cm (U.S. EPA, 1986a).

2. ABSORPTION FACTORS IN HUMANS AND EXPERIMENTAL ANIMALS

2.1. ORAL

Information regarding the absorption of naphthalene in humans and animals is limited. When ingested as a solid, naphthalene is sufficiently absorbed to cause toxicity in man (Chusid and Fried, 1955; Zuelzer and Apt, 1949; Nash, 1903; Gross et al., 1958; Haggerty, 1956). Furthermore, naphthalene seems to be more toxic when dissolved in oil before ingestion (Talakin, 1966). Summer et al. (1979) observed a dose-related increase in the 24-hour urinary excretion of thioethers by adult male SPF Wistar rats given single gavage doses of naphthalene in oil of 30-200 mg/kg. Urinary thioether accounted for 26-39% of the administered dose of naphthalene, which suggests 26-39% as a minimum estimate of the extent of gastrointestinal absorption. Bock et al. (1979) measured the uptake of radioactivity from the isolated in situ jejunum of rats given a dose of ^{14}C-naphthalene. Approximately 84% of the dose of radioactivity was found in the portal blood within 30 minutes of administration. These data suggest that gastrointestinal absorption of naphthalene in rats is both rapid and extensive. Sanborn and Halins (1977) suggested that naphthalene may be absorbed to a greater extent when ingested in water than in food.

2.2. INHALATION

Data regarding the absorption of inhaled naphthalene are limited; however, Valaes et al. (1963) reported toxicity and death in newborn infants exposed to naphthalene vapors from clothes or blankets that were stored in or near the infants' rooms.

3. TOXICITY IN HUMANS AND EXPERIMENTAL ANIMALS

3.1. SUBCHRONIC

3.1.1. Oral. Several investigators (Anziulewicz et al., 1959; Zinkham and Childs, 1958) reported the occurrence of hemolytic anemia in infants born to mothers who had "sniffed" and ingested unspecified quantities of naphthalene (in the form of mothballs) during pregnancy. The mothers themselves were also anemic, but to a lesser extent than were the infants.

Several animal studies focused upon ocular effects of naphthalene, but failed to mention whether any other signs of toxicity were measured or observed. Fitzhugh and Buschke (1949) observed slight cataracts in weanling rats exposed to 2% naphthalene in the diet for 60 days. Assuming a rat consumes food equivalent to 5% of its body weight/day, this dietary level is equivalent to a dose of 1 g/kg bw/day. In two separate studies, rabbits exposed to 1 g naphthalene/kg bw/day by gavage (either in light paraffin or an unspecified vehicle) for ~46 days developed cataracts (Ghetti and Mariani, 1956; Van Heyningen and Pirie, 1976) and degeneration of the retina (Van Heyningen and Pirie, 1976) within the first few days of treatment.

In an NTP (1980a) sponsored study, groups of 10 male and 10 female F344 rats were treated by gavage with naphthalene in corn oil at 0, 25, 50, 100, 200 or 400 mg/kg, 5 days/week for 13 weeks. At 400 mg/kg, two males died and rats of both sexes experienced diarrhea, lethargy, hunched posture and rough hair coats. A >10% decrease in body weight gain was observed in males at $\geq$200 mg/kg and in females at $\geq$100 mg/kg. Kidney lesions occurred in males at $\geq$200 mg/kg and lymphoid depletion of the thymus occurred in females at 400 mg/kg. Mild changes in hematologic parameters were observed in both sexes at 400 mg/kg. Eye lesions were not observed. The 50 mg/kg dosage was a NOEL in rats in this study.

A similar study was performed in groups of 10 male and 10 female B6C3F1 mice treated by gavage with naphthalene in corn oil at 0, 12.5, 25, 50, 100 or 200 mg/kg, 5 days/week for 13 weeks (NTP, 1980b). Seven mice (three males and two females of the 200 mg/kg group, one female of the 25 mg/kg group and one control male) died during the 2nd, 3rd and 4th weeks of the study from gavage trauma or accident. Transient signs of toxicity (lethargy, rough haircoats and decreased food consumption) occurred in both sexes at 200 mg/kg. Body weight gains of treated males exceeded controls; treated females had slight but probably not biologically significant dose-related decreases in body weight gain. There were no treatment-related histopathologic lesions or hematologic effects.

Shopp et al. (1984) administered naphthalene in corn oil by gavage to groups of 40-112 CD-1 mice/sex at 0 (untreated control), 0 (vehicle control), 5.3, 53 or 133 mg/kg/day for 90 consecutive days. There were no effects on survival, body weights, serum enzyme or electrolyte levels, or immunologic parameters, although females at 133 mg/kg/day had reduced absolute and relative spleen weights. There was no evidence of a naphthalene-induced hemolytic anemia, cataract formation or pathologic damage to the lungs. A dose-related inhibition of hepatic aryl hydrocarbon hydroxylase activity was observed in both sexes, but the toxicological significance of this observation is unclear.

3.1.2. Inhalation. Pertinent data regarding the subchronic toxicity of inhaled naphthalene were not located in the available literature.

3.2. CHRONIC

3.2.1. Oral. In the only chronic study available, Schmahl (1955) administered naphthalene in the diet to BDI and BDIII rats at a dose of 10-20 mg/rat/day for 700 days. The total cumulative dosage was 10 g/rat. The rats were observed until they died spontaneously; a comprehensive gross

and limited histopathologic examination was then performed. There were no treatment-related effects on survival (the lifespan of these rats exceeded 800 days) or on histopathology. No other signs of toxicity were reported.

3.2.2. Inhalation. Chronic data regarding the inhalation of naphthalene are limited to two studies of occupational exposure. Van der Hoeve (1906) reported that one man who worked with powdered naphthalene developed cataracts and retinal hemorrhage, while another man exposed similarly had chorioretinitis. Ghetti and Mariani (1956) reported that 8/21 workers exposed to unspecified "high" concentrations of naphthalene in a dye-manufacturing process developed cataracts. Since these men were <50 years of age, it is unlikely that they would have developed cataracts spontaneously.

3.3. TERATOGENICITY AND OTHER REPRODUCTIVE EFFECTS

3.3.1. Oral. Matorova and Chetverikova (1981) administered naphthalene by gavage at 0.075, 0.15 or 70 mg/kg/day to pregnant white mongrel rats on days 1-19 of gestation. There is a discrepency in this paper in that in the abstract the highest dose is listed a 7 mg/kg/day. However, 70 mg/kg/day is consistently specified in the remainder of the paper. The rats were sacrificed for examination on gestation day 19. No grossly visible developmental defects were observed at any dosage and no microscopic anomalies were noted at 0.075 mg/kg/day. At $\geq$0.15 mg/kg/day, there was an increased incidence of fetuses with subcutaneous hematomas; embryonic mortality and preimplantation loss were also increased. The length of gestation in rats allowed to deliver appeared to be increased to up to 27 days in the treated groups. At $\geq$0.15 mg/kg/day, rats were born with black tails that fell off 6-8 hours later.

Plasterer et al. (1985) administered naphthalene in corn oil by gavage to 50 mated CD-1 mice at 300 mg/kg/day on days 7-14 of gestation. A vehicle control group was maintained. Maternal toxicity was manifested as increased mortality and reduced body weight gain. Fetal toxicity was manifested as a

reduced number of live young at birth, which the authors attributed to early fetal resorptions. The young were not examined for terata.

Naphthalene or its metabolites are known to cross the placenta in sufficient quantities to cause fetotoxic effects (Anziulewicz et al., 1959; Van der Hoeve, 1913). These effects included hemolytic anemia in humans and cataracts and retinal damage in rabbits. Doses either were not estimated or were not reported in the secondary sources. The i.p. injection of 395 mg/kg/day naphthalene in corn oil to Sprague-Dawley rats on days 1-15 of gestation did not result in any evidence of maternal or fetotoxicity (Hardin et al., 1981).

3.3.2. Inhalation. Pertinent data regarding the teratogenicity of inhaled naphthalene were not located in the available literature.

3.4. TOXICANT INTERACTIONS

A woman exposed for 3 weeks to a combination of naphthalene and para-dichlorobenzene (while mothproofing clothing) developed aplastic anemia 1 month after exposure (Harden and Baetjer, 1978). No other cases of aplastic anemia associated with exposure to either napthalene or paradichlorobenzene alone have been reported in the literature.

4. CARCINOGENICITY

4.1. HUMAN DATA

4.1.1. Oral. Pertinent data regarding the carcinogenicity of ingested naphthalene in humans were not located in the available literature.

4.1.2. Inhalation. Wolf (1976) reported that 6/15 workers exposed for up to 32 years to vapors of both naphthalene and coal tar developed laryngeal carcinomas (4) or neoplasms of the pylorus and cecum (2). There was no control group.

4.2. BIOASSAYS

4.2.1. Oral. Schmahl (1955) investigated the carcinogenic potential of napthalene administered orally in rat strains BDI and BDII. A group of 28 rats were exposed to 10-20 mg/day in the feed for 700 days (total cumulative dose of 10 g naphthalene/rat) and monitored for up to 1000 days. A carcinogenic response was not observed.

4.2.2. Inhalation. Adkins et al. (1986) tested naphthalene in the mouse pulmonary adenoma induction test using groups of 30 female strain A/J mice at 6-8 weeks of age. Exposure to 0, 10 or 30 ppm (0, 52 or 157 mg/m^3), 6 hours/day, 5 days/week for 6 months did not elicit a carcinogenic response. Positive controls consisted of 20 female mice given a single intraperitonal injection of urethane and sacrificed after a 26-week observation period. All positive controls developed tumors. NTP (1987) is currently examining the effects of 10 and 30 ppm napthalene on mice in a 2-year inhalation study.

4.3. OTHER RELEVANT DATA

The genotoxic activity of naphthalene has been tested in several *in vitro* systems. Cell transformation was not seen in rodent embryo cells pretreated with leukemia virus and exposed to concentrations of naphthalene up to 100 mg/L of culture medium (Freeman et al., 1973; Rhim et al., 1974). Similarly, cell transformations were not seen in a murine mammary

gland organ culture system at naphthalene concentrations up to 1000 mg/ℓ of culture medium (Tonelli et al., 1979). Naphthalene did not cause DNA damage in a rat hepatocyte alkaline elution assay (Sina et al., 1983).

Naphthalene was not found to be mutagenic in a number of bacterial/microsomal assay systems (McCann et al., 1975; Kraemer et al., 1974; Mortelmans et al., 1986).

Knake (1956) administered coal tar napthalene in sesame oil subcutaneously to 40 white rats every 2 weeks for 7 doses, and observed the rats for 18 months. A control group of 40 rats received injections of corn oil alone. Carbolfuchsin, a known carcinogen, was painted on the skin before injection. The naphthalene contained impurities that were equivalent to 10% methyl naphthalene. Thirty-four of 40 naphthalene treated rats survived to termination and 5 of these developed invasive or metastatic lymphosarcomas. In the controls, 32 survived and only 1 developed lymphosarcoma. In a skin painting study, Knake (1956) applied coal tar naphthalene in benzene or benzene alone to inbred black mice 5 days/week for life. Lymphatic leukemia developed in 4/25 naphthalene treated mice compared with 0/21 in benzene treated controls and 5/1227 historical controls.

Naphthalene was negative for induction of γ-GT foci, which was considered to be a preneoplastic response, in the livers of partially hepatectomized rats (Tsuda et al., 1980). U.S. EPA (1980a, 1986a) listed other studies which were insufficiently reported or otherwise flawed, that provided no evidence of carcinogenicity for naphthalene (Boyland et al., 1964; Kennaway, 1930; Kennaway and Heiger, 1930; Bogdat'eva and Bid, 1955; Schmeltz et al., 1978).

4.4. WEIGHT OF EVIDENCE

IARC has not evaluated the risk to humans that is associated with oral or inhalation exposure to naphthalene. Naphthalene was negative for carcinogenicity in oral (Schmahl, 1955; Druckrey and Schmahl, 1955) and inhalation (Adkins et al., 1986). However, each of these studies individually appear to have been inadequately designed. Applying the criteria for evaluating the overall weight of evidence for carcinogenicity adopted by the EPA (U.S. EPA, 1986c), the evidence for carcinogenicity of naphthalene in humans and animals is inadequate and the chemical is designated as Group D -- not classifiable as to carcinogenicity to humans. This qualitative assessment is consistent with that of U.S. EPA (1986a). The assessment should be reevaluated pending the final results of the NTP bioassay of naphthalene.

5. REGULATORY STANDARDS AND CRITERIA

The ACGIH (1986a) has recommended a TLV-TWA of 10 ppm (50 mg/m^3) and a STEL of 15 ppm (75 mg/m^3) for occupational exposure to naphthalene. Since eye irritation was seen at 15 ppm, this criterion was chosen "to prevent ocular effects but possibly not blood changes in hypersusceptibles" (ACGIH, 1986b). The OSHA (1985) standard for exposure to naphthalene in the workplace is a PEL of 10 ppm (50 mg/m^3).

6. RISK ASSESSMENT

6.1. SUBCHRONIC REFERENCE DOSE (RfD_S)

6.1.1. Oral (RfD_{SO}). The only subchronic oral studies that were sufficient to be considered for risk assessment are the NTP (1980a,b) 90-day gavage studies (rats and mice) and the Shopp et al. (1984) 90-day gavage study (mice). Rats appear to be somewhat more sensitive than mice to naphthalene and, therefore, are selected as the model of choice for deriving an RfD_{SO}. Rats were treated with naphthalene in corn oil at 0, 25, 50, 100, 200 or 400 mg/kg, 5 days/week (NTP, 1980a). Gross signs of toxicity and mortality occurred in both sexes at 400 mg/kg, histopathologic lesions and reduced body weight gain occurred in both sexes at 200 mg/kg, reduced body weight gain occurred in females at 100 mg/kg, and 50 mg/kg appeared to be a NOEL. When the NOEL of 50 mg/kg is multiplied by 5/7 to expand from treatment on 5 days/week to daily treatment, it corresponds to a transformed dose of 36 mg/kg/day.

Application of an uncertainty factor of 100, 10 to extrapolate from rats to humans and 10 to protect more sensitive humans, to the NOEL of 36 mg/kg/day would result in an RfD_{SO} of 0.36 mg/kg/day, which is lower than the chronic RfD_O derived in Section 6.2.1. The subchronic NTP (1980a) rat study, therefore, is not chosen as the basis for an RfD_{SO} but is considered to support the chronic oral NOEL of 41 mg/kg/day in the Schmahl (1955) study that served as the basis for the chronic RfD_O. Because of the similarity in the chronic and subchronic NOELs, the chronic RfD of 0.4 mg/kg/day or 29 mg/day from the Schmahl (1955) study is adopted as the RfD_{SO} for naphthalene. Medium confidence is placed in this RfD_{SO}, as discussed in Section 6.2.1.

6.1.2. Inhalation (RfD_{SI}). The lack of pertinent, quantitative data precludes assessment of risk associated with inhalation of naphthalene.

6.2. REFERENCE DOSE (RfD)

6.2.1. Oral (RfD_0). The only chronic oral study located in the available literature was the dietary cancer study by Schmahl (1955) in which rats received a total dose of 10 g of naphthalene over a 700-day period. Assuming a reference body weight for rats of 0.35 kg, naphthalene was consumed at a dosage rate of 41 mg/kg/day. No effects were observed in the treated rats. The NOEL of 41 mg/kg/day is supported by the NOEL for rats of 36 mg/kg/day in the subchronic NTP (1980a) gavage study. Application of an uncertainty factor of 100, 10 to extrapolate from rats to humans and 10 to protect more sensitive humans, results in an RfD_0 of 0.4 mg/kg/day or 29 mg/day for a 70 kg human. This analysis in consistent with an earlier U.S. EPA (1986a) derivation. Confidence in the data base is medium because the carcinogenicity, developmental and reproductive toxicity have not been investigated sufficiently. Confidence in the key study is low because only one dosage level was tested, histopathologic examination was limited and dosing was not precisely controlled. Because of the support provided by the NTP (1980a,b) and Shopp et al. (1984) studies, confidence in the RfD_0 is rated medium. Naphthalene is currently listed as under review by the RfD workgroup.

U.S. EPA (1986a) derived a CS for naphthalene from the subchronic NTP (1980a) gavage study. Histopathologic lesions were observed in the kidneys of male rats treated with 200 mg/kg, 5 days/week (143 mg/kg/day). An uncertainty factor of 10 was applied to expand from subchronic to chronic exposure. From an estimated rat body weight of 0.31 kg, a human MED of 164.4 mg/day was calculated, which corresponds to an RV_d of 2.2. An RV_e of 6 was chosen to represent the kidney lesions and the CS was calculated as 13.2. This CS is adopted for the purposes of this document.

6.2.2. Inhalation (RfD_I). Data regarding chronic exposure to naphthalene by inhalation were not located in the available literature. NTP (1987) is currently examining the effects of 10 and 30 ppm naphthalene on mice in a 2-year inhalation study (see Section 6.3.2.).

6.3. CARCINOGENIC POTENCY (q_1^*)

6.3.1. Oral. Naphthalene has not been adequately tested in animal bioassays; therefore, it is not possible to derive a q_1^* for oral exposure to naphthalene.

6.3.2. Inhalation. The lack of pertinent data regarding the carcinogenicity of inhaled naphthalene precludes assessment of carcinogenic potency. NTP (1987) is currently examining the effects of 10 and 30 ppm naphthalene on mice in a 2-year inhalation study. Preliminary results have been submitted to the EPA, and upon peer review by the NTP Board of Scientific Counselors, the EPA will evaluate the results to determine if any changes in the current regulatory assessment are warranted (U.S. EPA, 1988).

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APPENDIX

Summary Table for Naphthalene

	Species	Experimental Dose/Exposure (mg/kg/day)	Effect	Reference Dose (RfD or RfD_S)	Reference
Inhalation					
RfD_{SI} (formerly AIS)	ID	ID	ID	ID	ID
RfD_I (formerly AIC)	ID	ID	ID	ID	ID
Oral					
RfD_{SO}	rat	10 g total dose over 700 days (41 mg/kg/day)	NOEL	29 mg/day	Schmahl, 1955
RfD_O	rat	10 g total dose over 700 days (41 mg/kg/day)	NOEL	29 mg/day	Schmahl, 1955; U.S. EPA, 1986a
Maximum CS	rat	200 mg/day, 5 days/week by gavage for 90 days (143 mg/kg/day) (RV_d = 2.2)	kidney lesions (RV_e=6)	CS = 13.2	NTP, 1980a; U.S. EPA, 1986a

ID = Insufficient data